FIG. 1

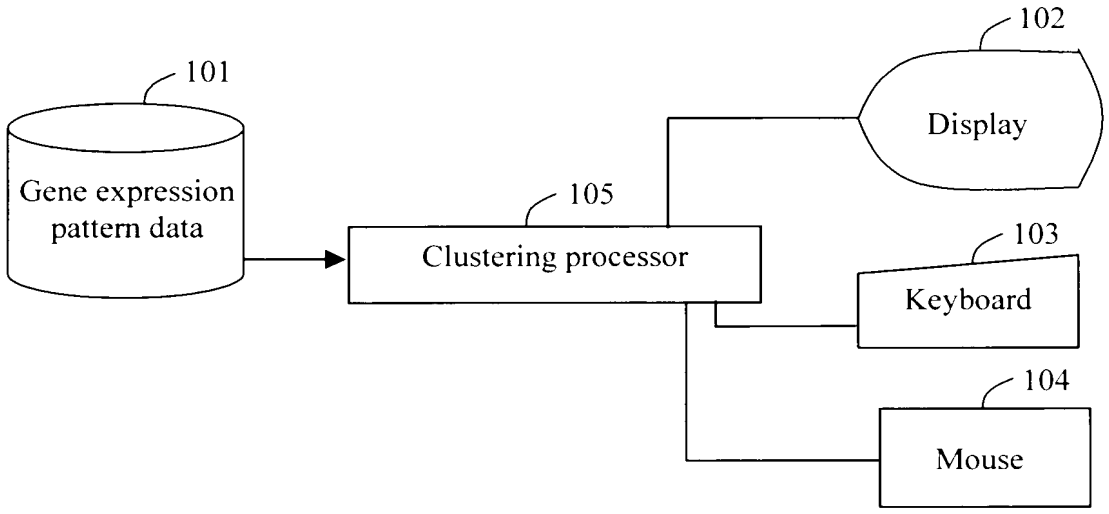
101
Gene expression pattern data
102
Display
105
Clustering processor
103
Keyboard
104
Mouse

FIG. 2

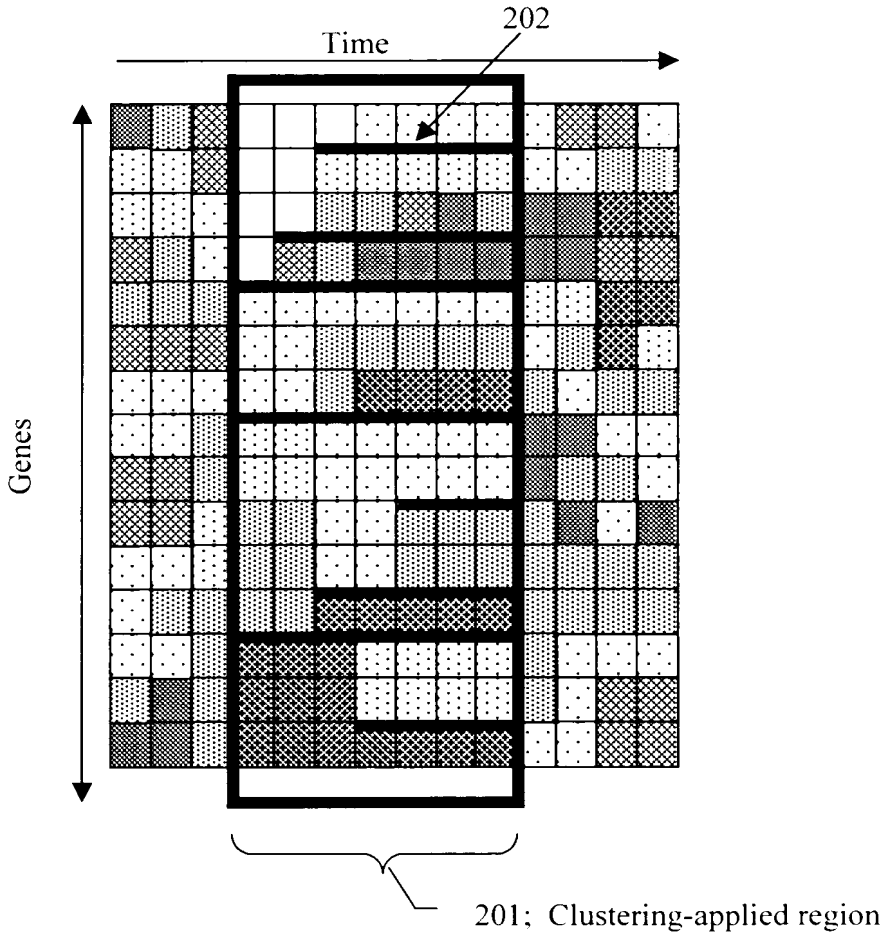

FIG.3

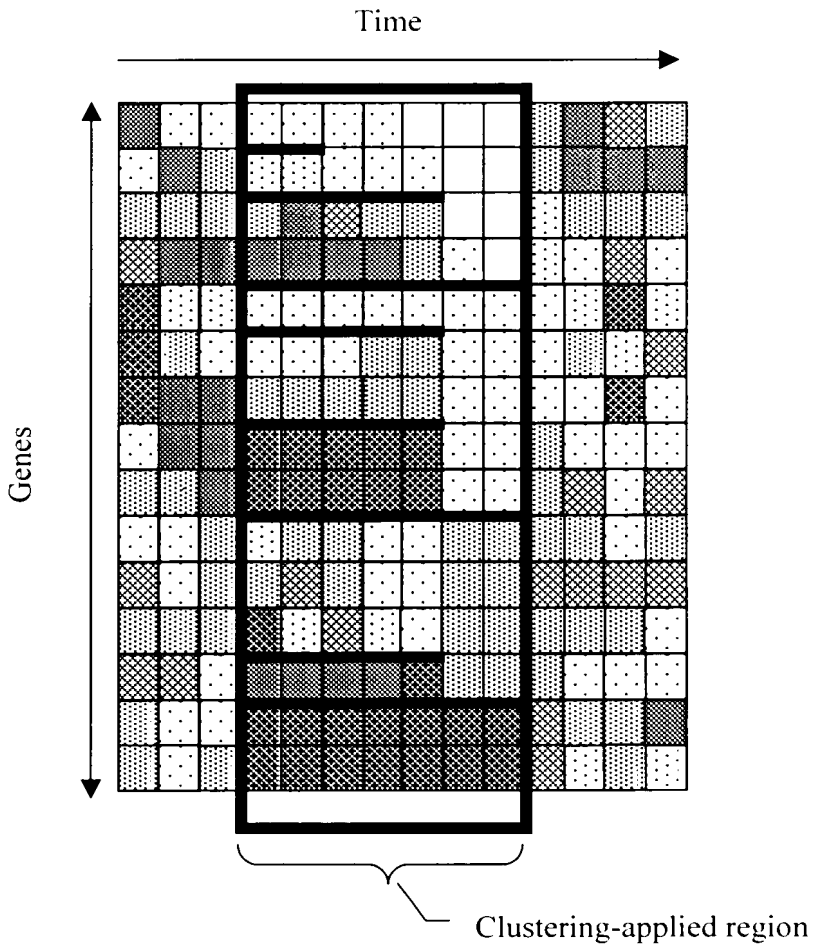

FIG. 4

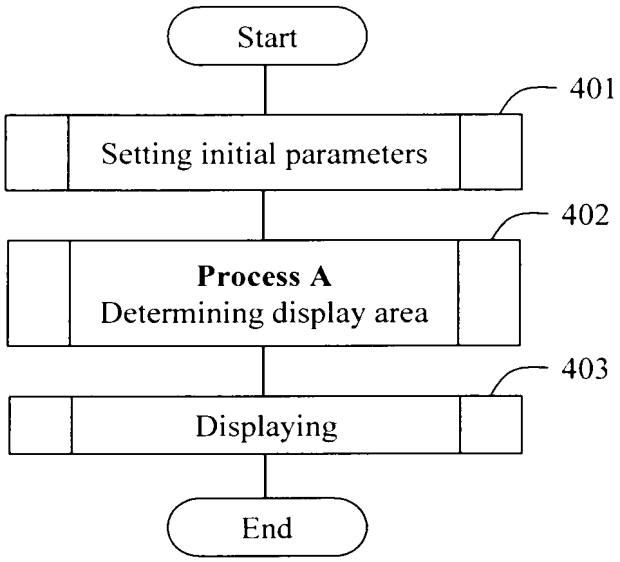
Start
401
Setting initial parameters
402
Process A
Determining display area
403
Displaying
End

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FIG. 5

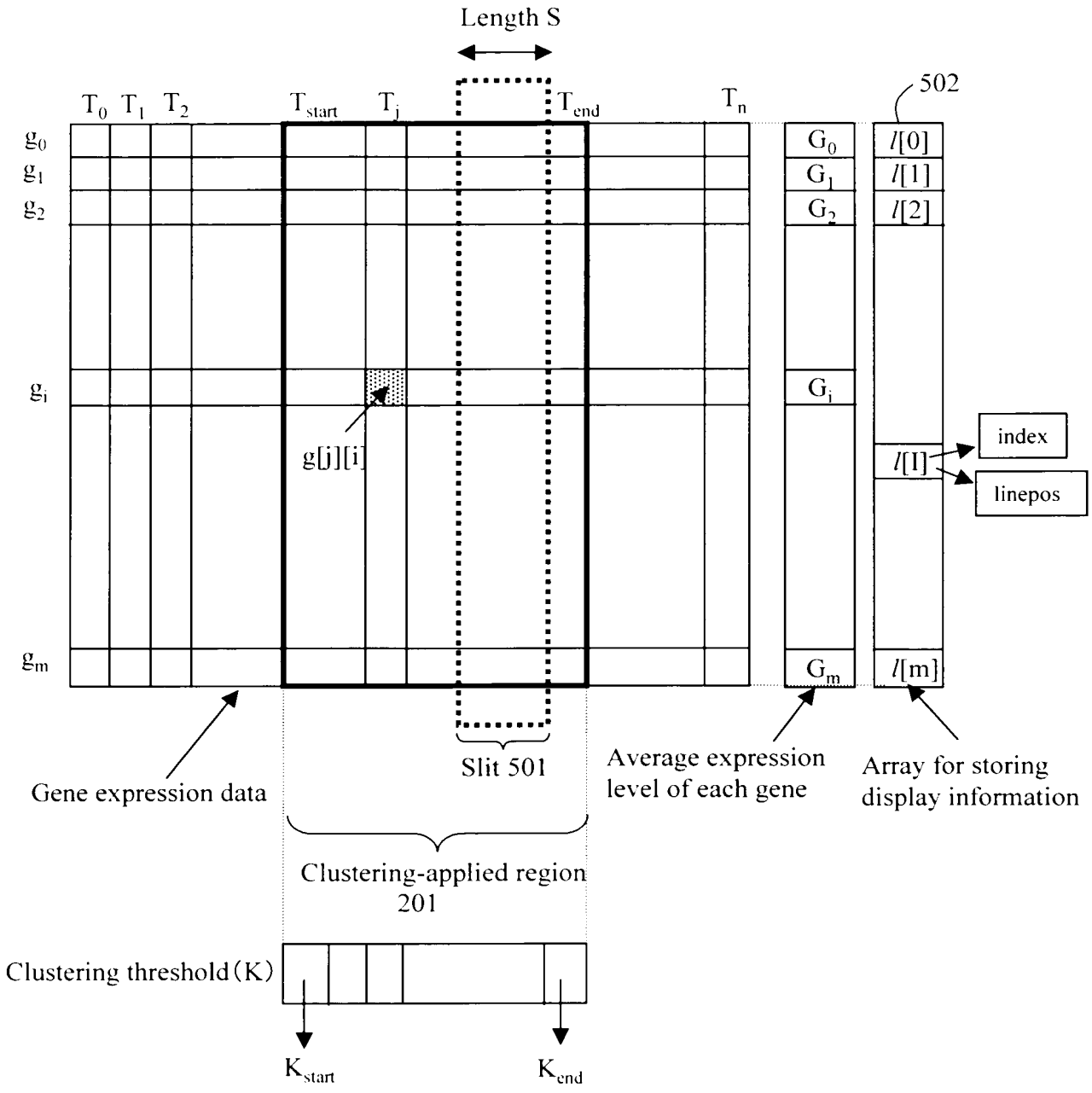

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FIG. 6

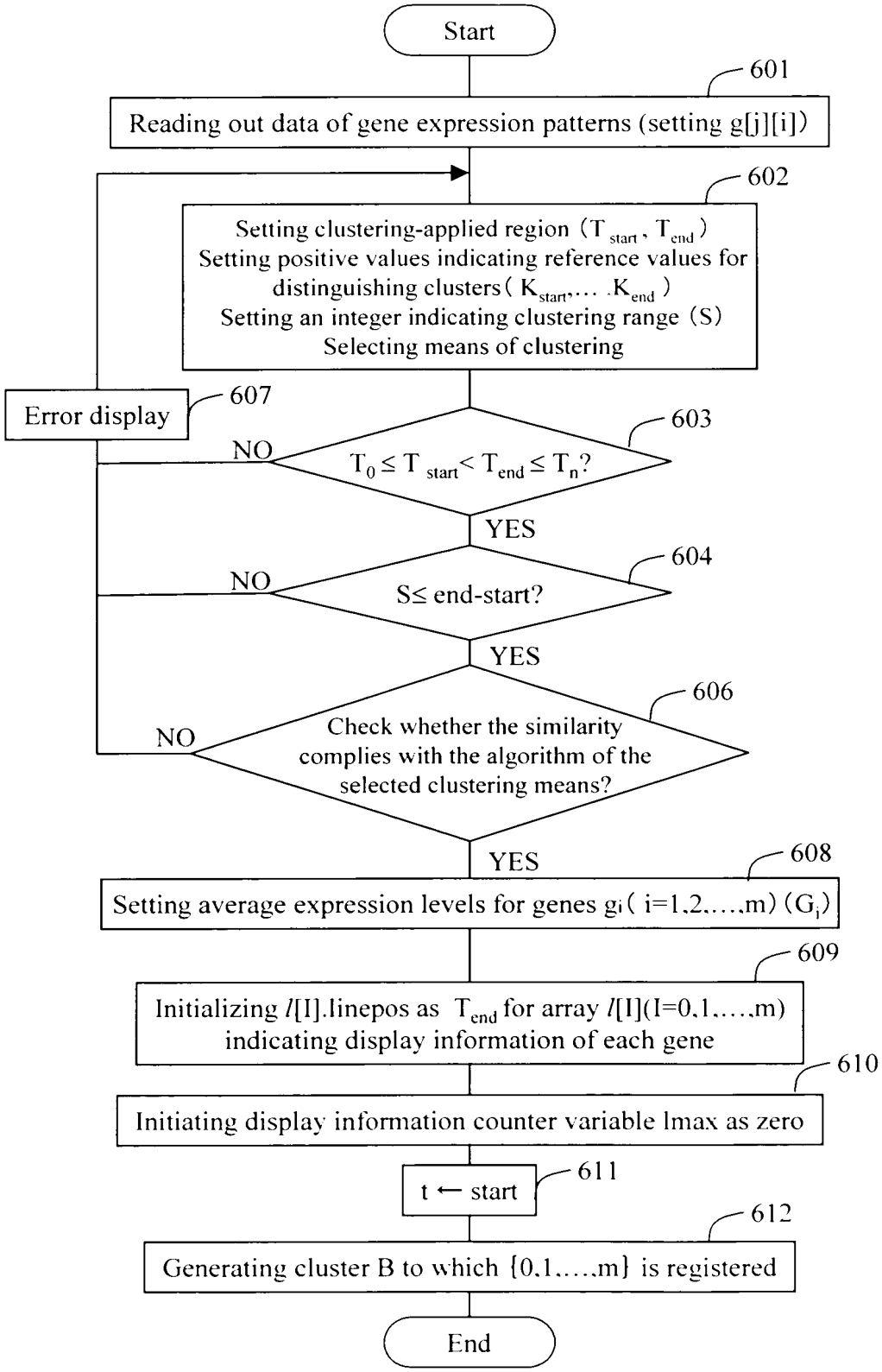

FIG. 7

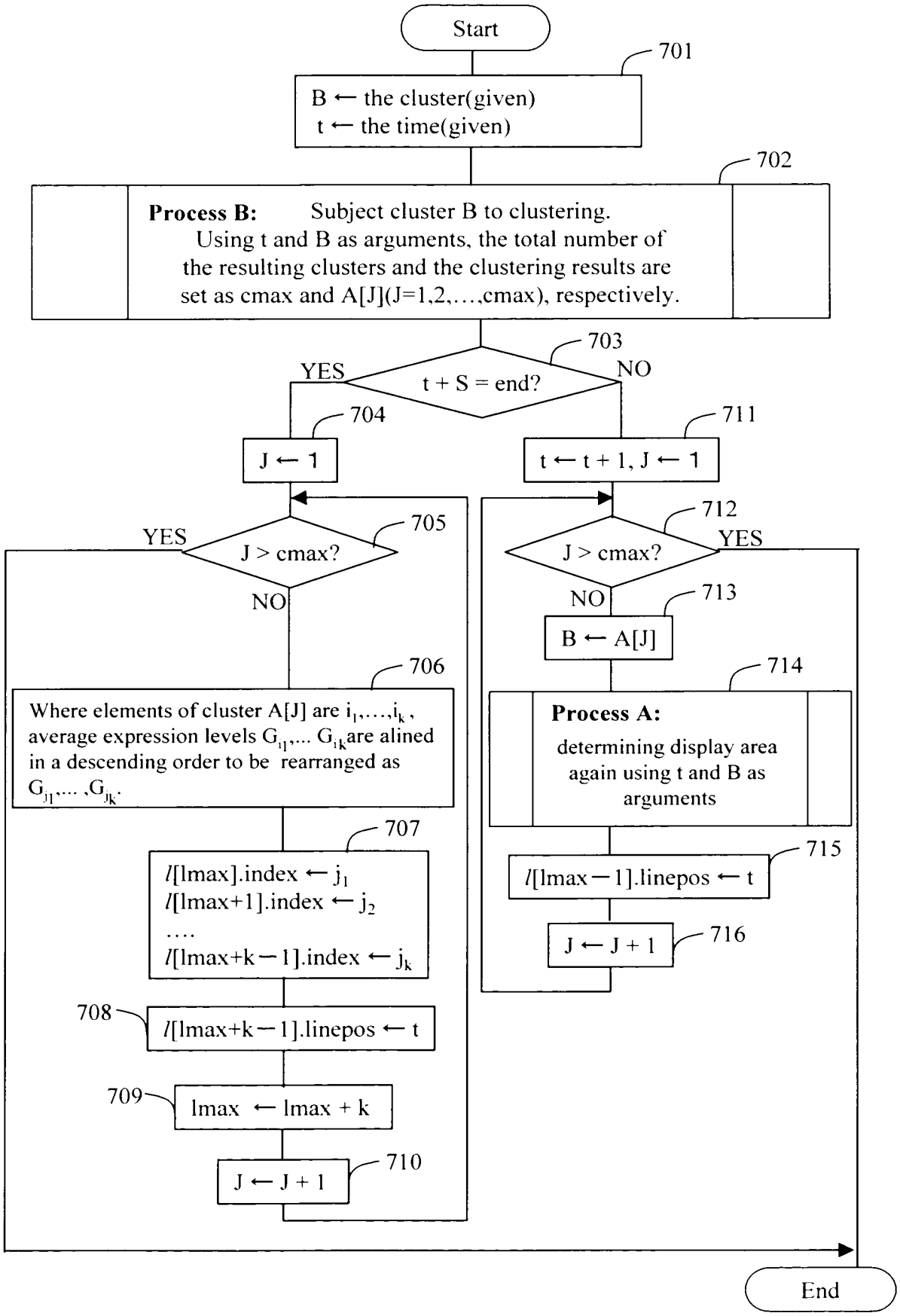
Start
701
B ← the cluster(given)
t ← the time(given)
702
Process B: Subject cluster B to clustering.
Using t and B as arguments, the total number of the resulting clusters and the clustering results are set as cmax and A[J](J=1,2,…,cmax), respectively.
703
t + S = end?
YES
NO
704
J ← 1
711
t ← t + 1, J ← 1
705
J > cmax?
YES
NO
712
J > cmax?
YES
NO
713
B ← A[J]
706
Where elements of cluster A[J] are $i_1,\ldots,i_k$, average expression levels $G_{i1},\ldots G_{ik}$ are alined in a descending order to be rearranged as $G_{j1},\ldots,G_{jk}$.
714
Process A:
determining display area again using t and B as arguments
707
l[lmax].index ← j_1
l[lmax+1].index ← j_2
….
l[lmax+k−1].index ← j_k
715
l[lmax−1].linepos ← t
716
J ← J + 1
708
l[lmax+k−1].linepos ← t
709
lmax ← lmax + k
710
J ← J + 1
End

FIG. 8

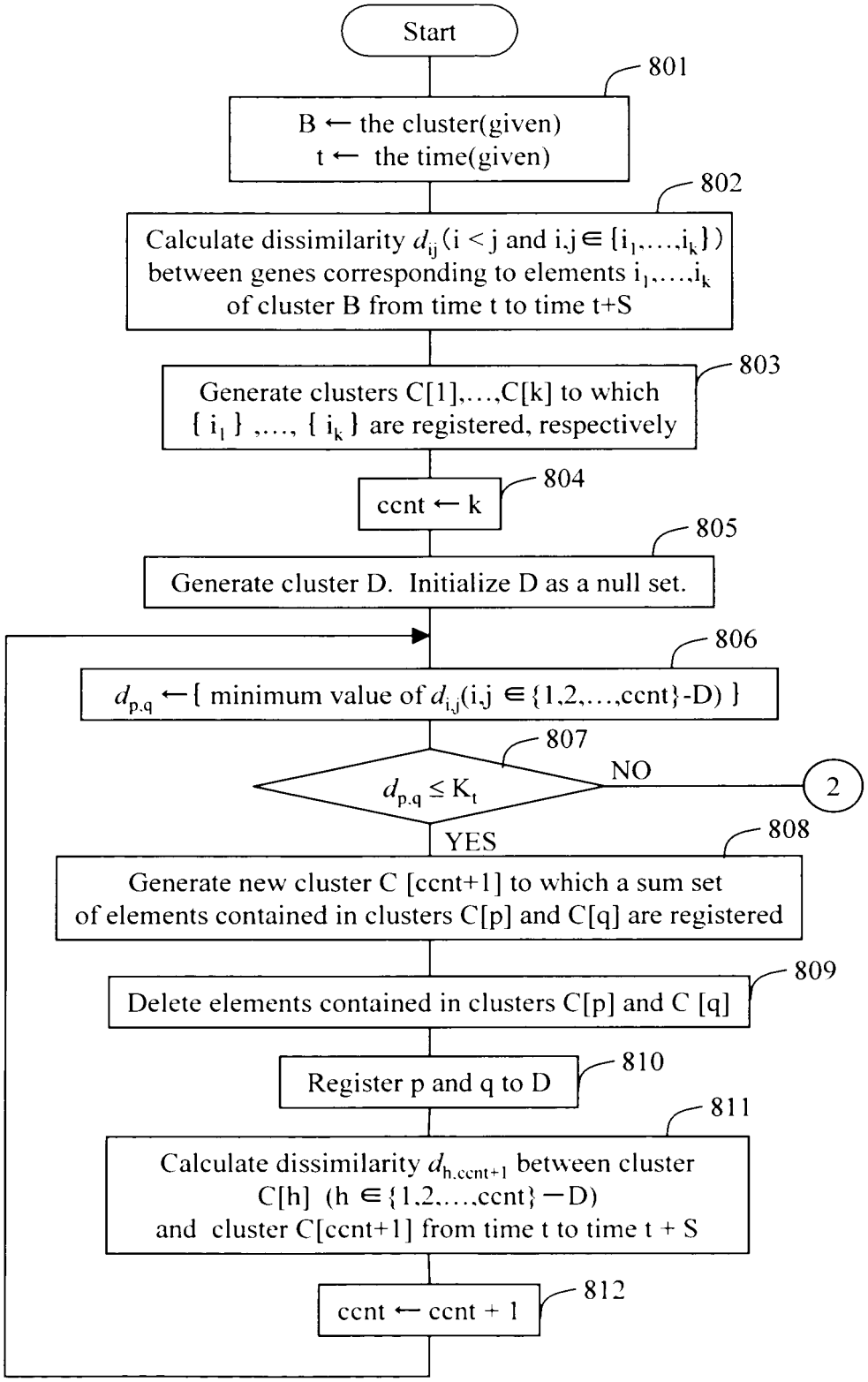
Start
801
B ← the cluster(given)
t ← the time(given)
802
Calculate dissimilarity d_{ij} (i < j and i,j ∈ {i_1,…,i_k}) between genes corresponding to elements i_1,…,i_k of cluster B from time t to time t+S
803
Generate clusters C[1],…,C[k] to which { i_1 } ,…, { i_k } are registered, respectively
804
ccnt ← k
805
Generate cluster D. Initialize D as a null set.
806
$d_{p,q}$ ← { minimum value of $d_{i,j}$(i,j ∈ {1,2,…,ccnt}-D) }
807
$d_{p,q} \le K_t$
NO
2
YES
808
Generate new cluster C [ccnt+1] to which a sum set of elements contained in clusters C[p] and C[q] are registered
809
Delete elements contained in clusters C[p] and C [q]
810
Register p and q to D
811
Calculate dissimilarity $d_{h,ccnt+1}$ between cluster C[h] (h ∈ {1,2,…,ccnt} − D) and cluster C[ccnt+1] from time t to time t + S
812
ccnt ← ccnt + 1

FIG. 9

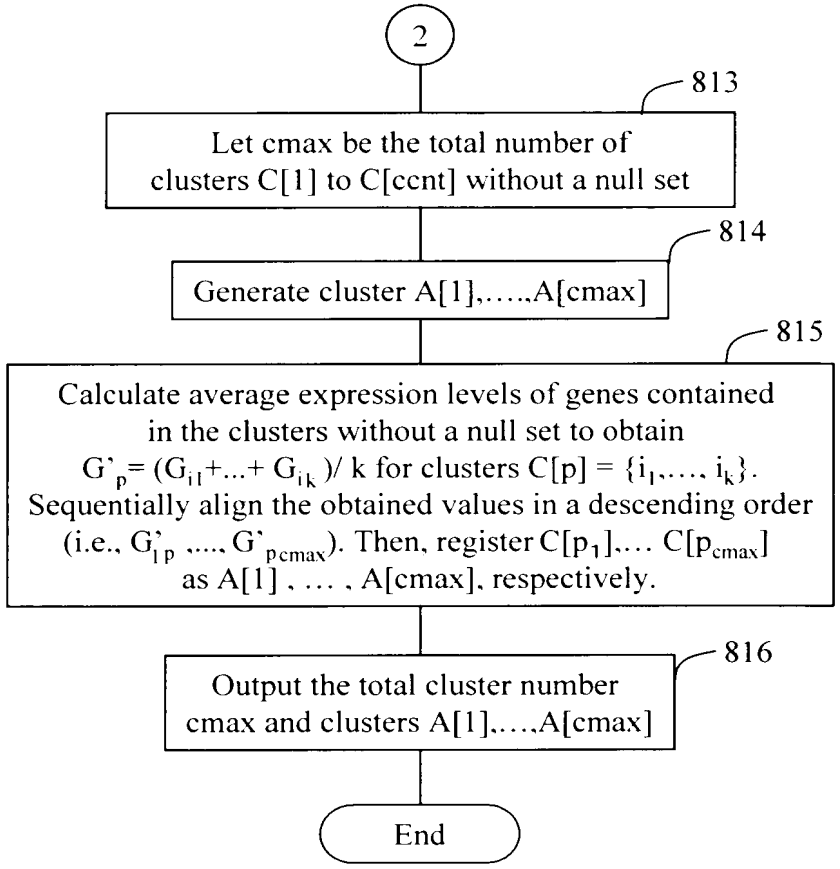
2
813
Let cmax be the total number of clusters C[1] to C[ccnt] without a null set
814
Generate cluster A[1],....,A[cmax]
815
Calculate average expression levels of genes contained in the clusters without a null set to obtain G'p= (Gi1+...+ Gik)/ k for clusters C[p] = {i1,.... ik}. Sequentially align the obtained values in a descending order (i.e., G'1p ,...., G'pcmax). Then, register C[p1],... C[pcmax] as A[1] , ... , A[cmax], respectively.
816
Output the total cluster number cmax and clusters A[1],...,A[cmax]
End

FIG. 10

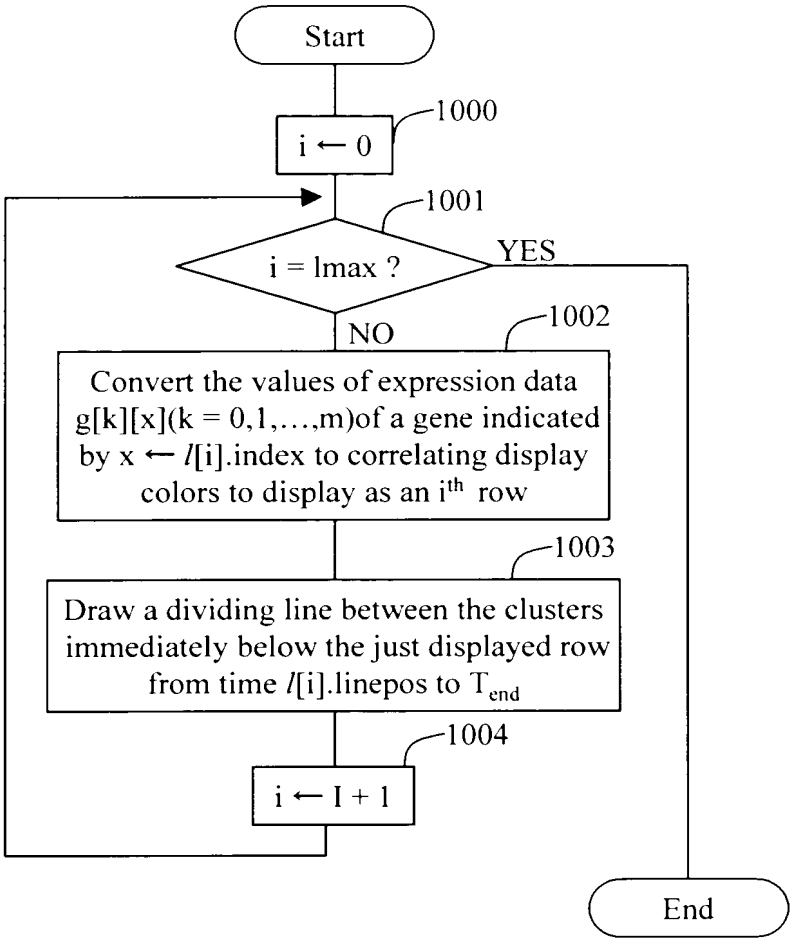
Start
1000
i ← 0
1001
i = lmax ?
YES
NO
1002
Convert the values of expression data g[k][x](k = 0,1,…,m)of a gene indicated by x ← l[i].index to correlating display colors to display as an i^th row
1003
Draw a dividing line between the clusters immediately below the just displayed row from time l[i].linepos to T_end
1004
i ← I + 1
End

FIG.11

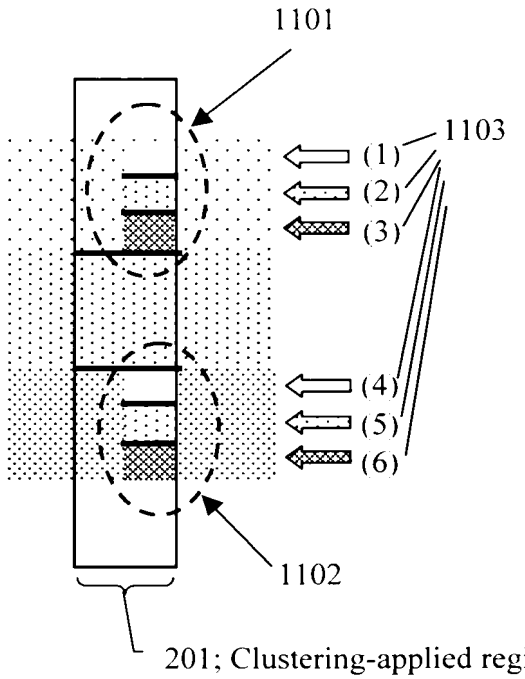

FIG.12

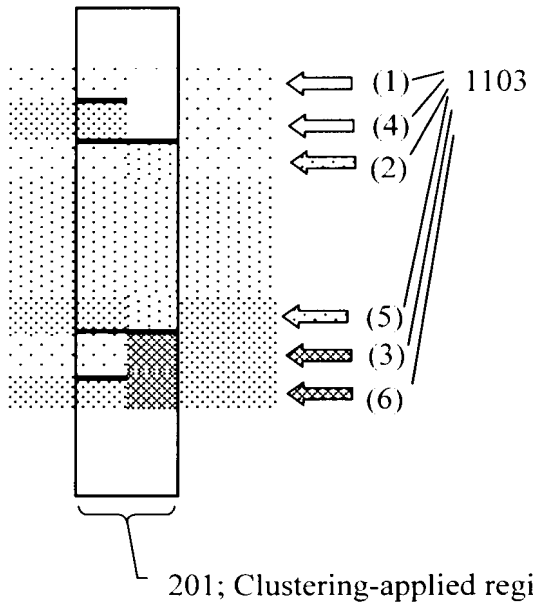

FIG.13

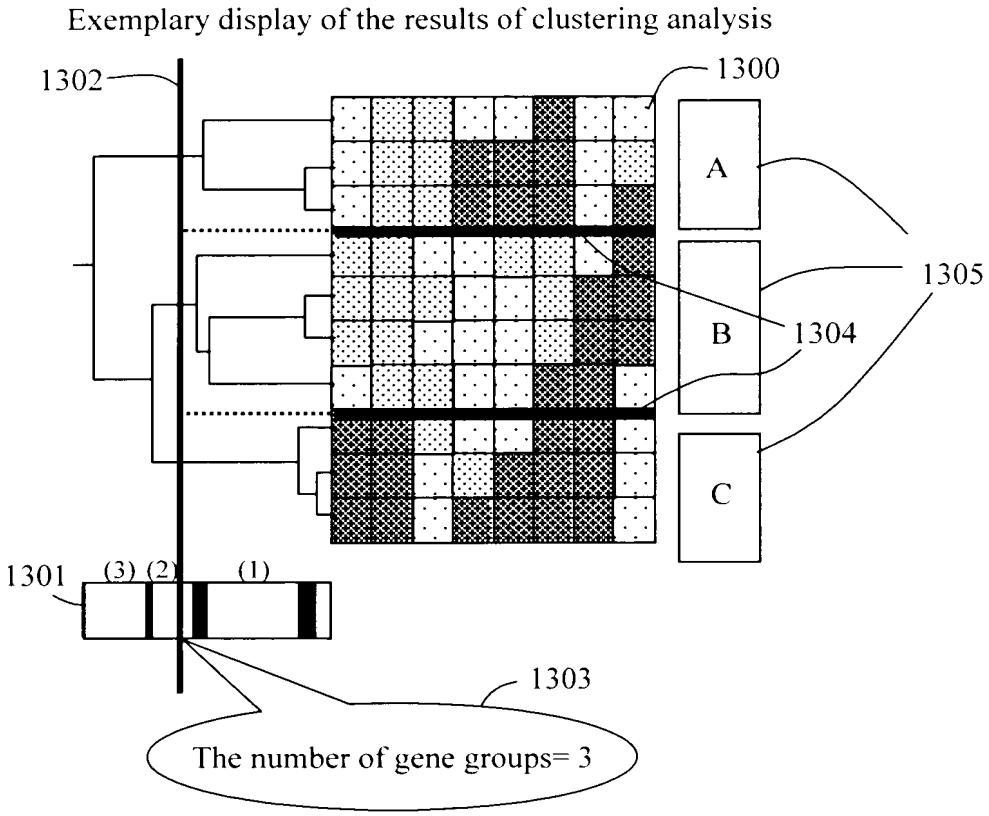
Exemplary display of the results of clustering analysis
1302
1300
A
B
C
1305
1304
1301
(3) (2)
(1)
1303
The number of gene groups= 3

FIG.14

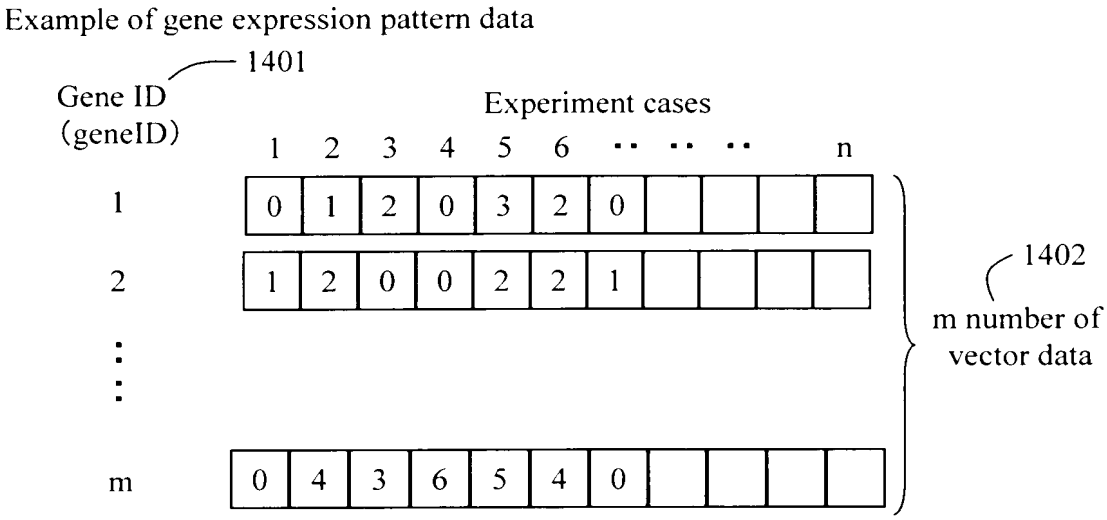
Example of gene expression pattern data
1401
Gene ID
(geneID)
Experiment cases
1 2 3 4 5 6 .. .. .. n
1
0 1 2 0 3 2 0
2
1 2 0 0 2 2 1
m
0 4 3 6 5 4 0
1402
m number of
vector data

FIG.15

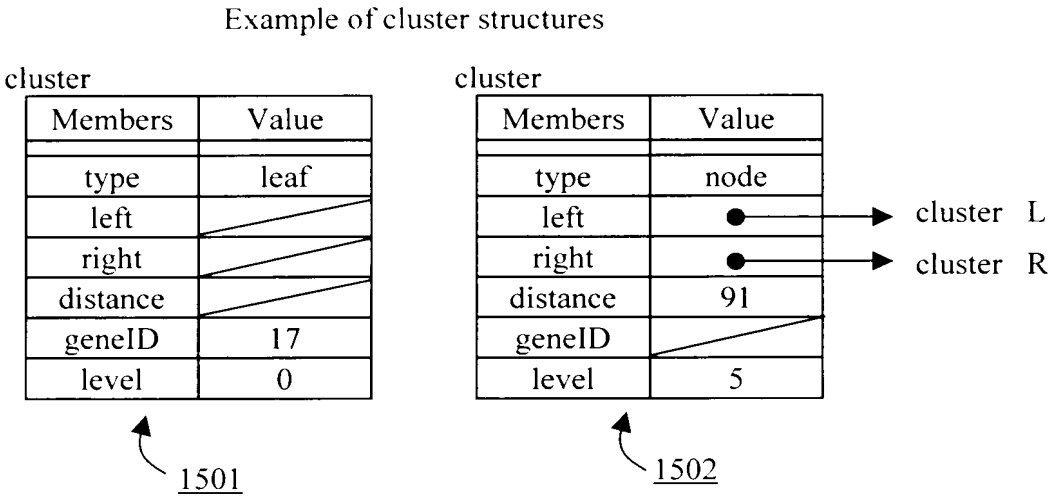
Example of cluster structures
cluster
Members
Value
type
leaf
left
right
distance
geneID
17
level
0
1501
cluster
Members
Value
type
node
left
right
distance
91
geneID
level
5
1502
cluster L
cluster R

FIG.16

Exemplary structure of cluster tree

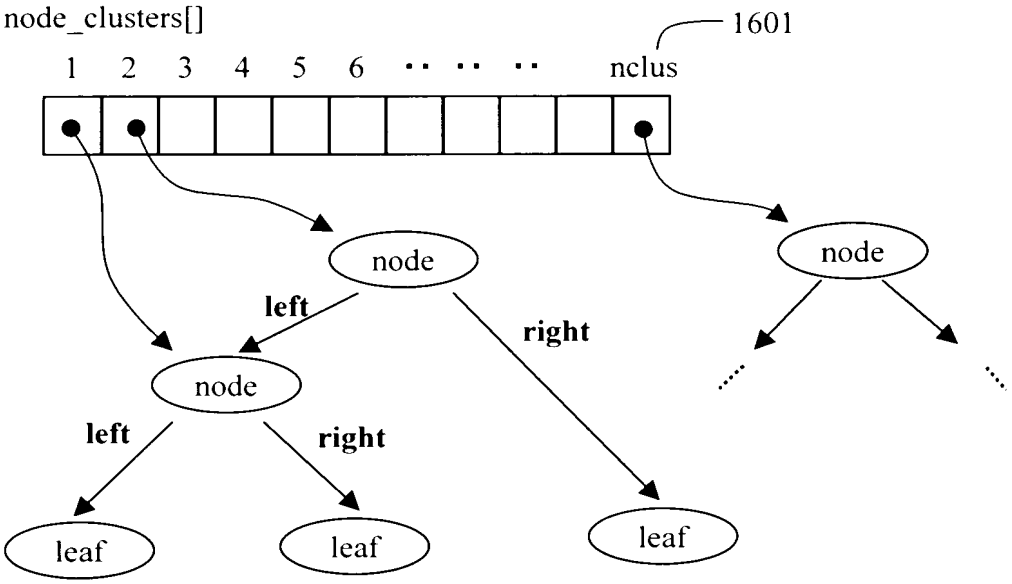

FIG.17

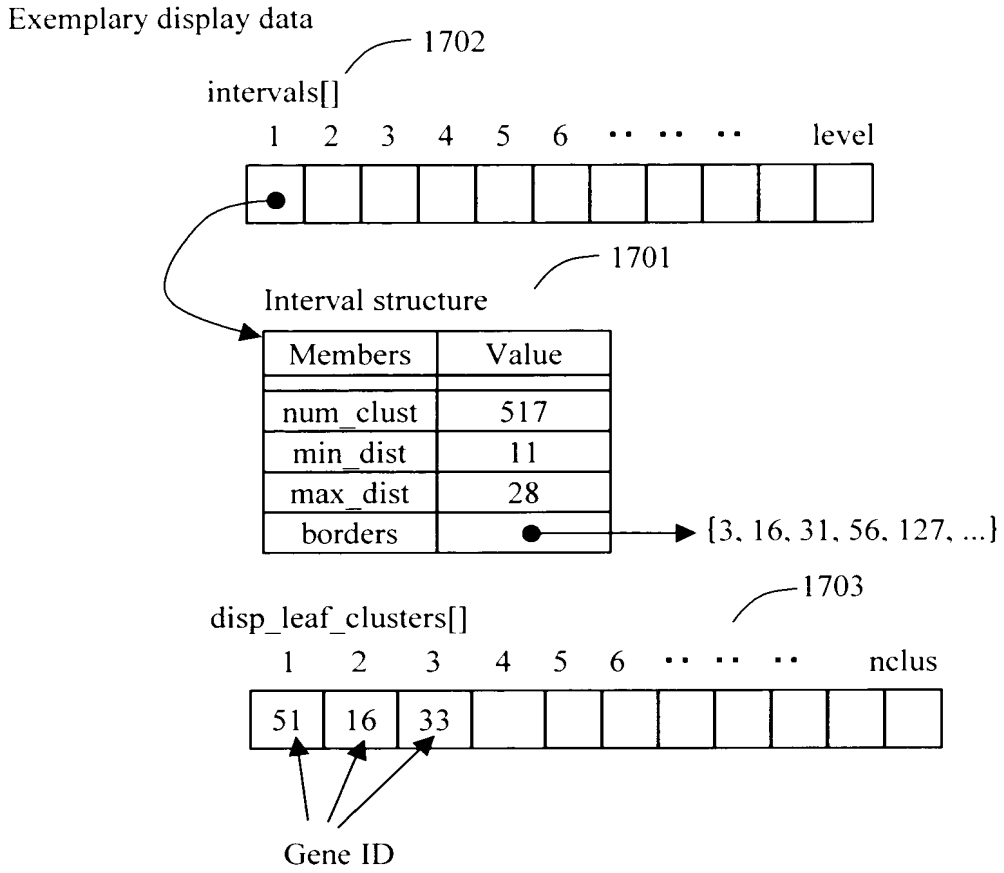
Exemplary display data
1702
intervals[]
1 2 3 4 5 6 • • • • • • level
1701
Interval structure
Members
Value
num_clust
517
min_dist
11
max_dist
28
borders
{3, 16, 31, 56, 127, ...}
1703
disp_leaf_clusters[]
1 2 3 4 5 6 • • • • • • nclus
51
16
33
Gene ID

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FIG.18

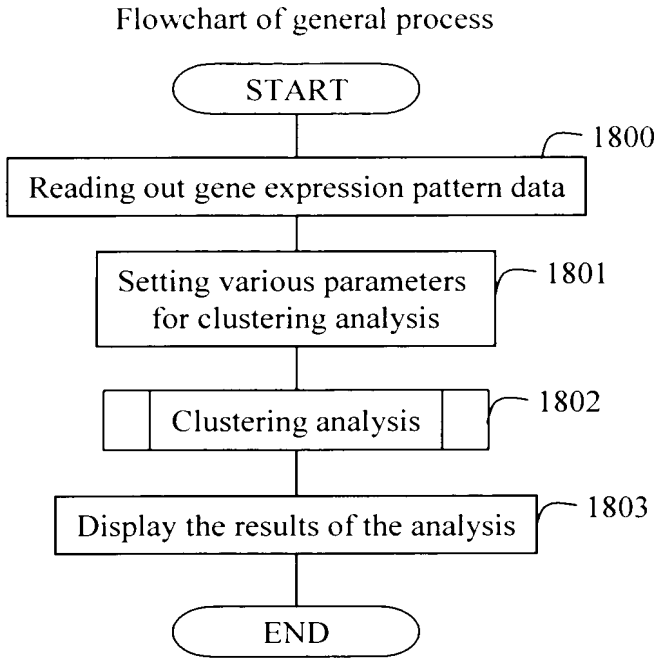

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FIG.19

Detailed flowchart of clustering analysis (1: Generating cluster tree)

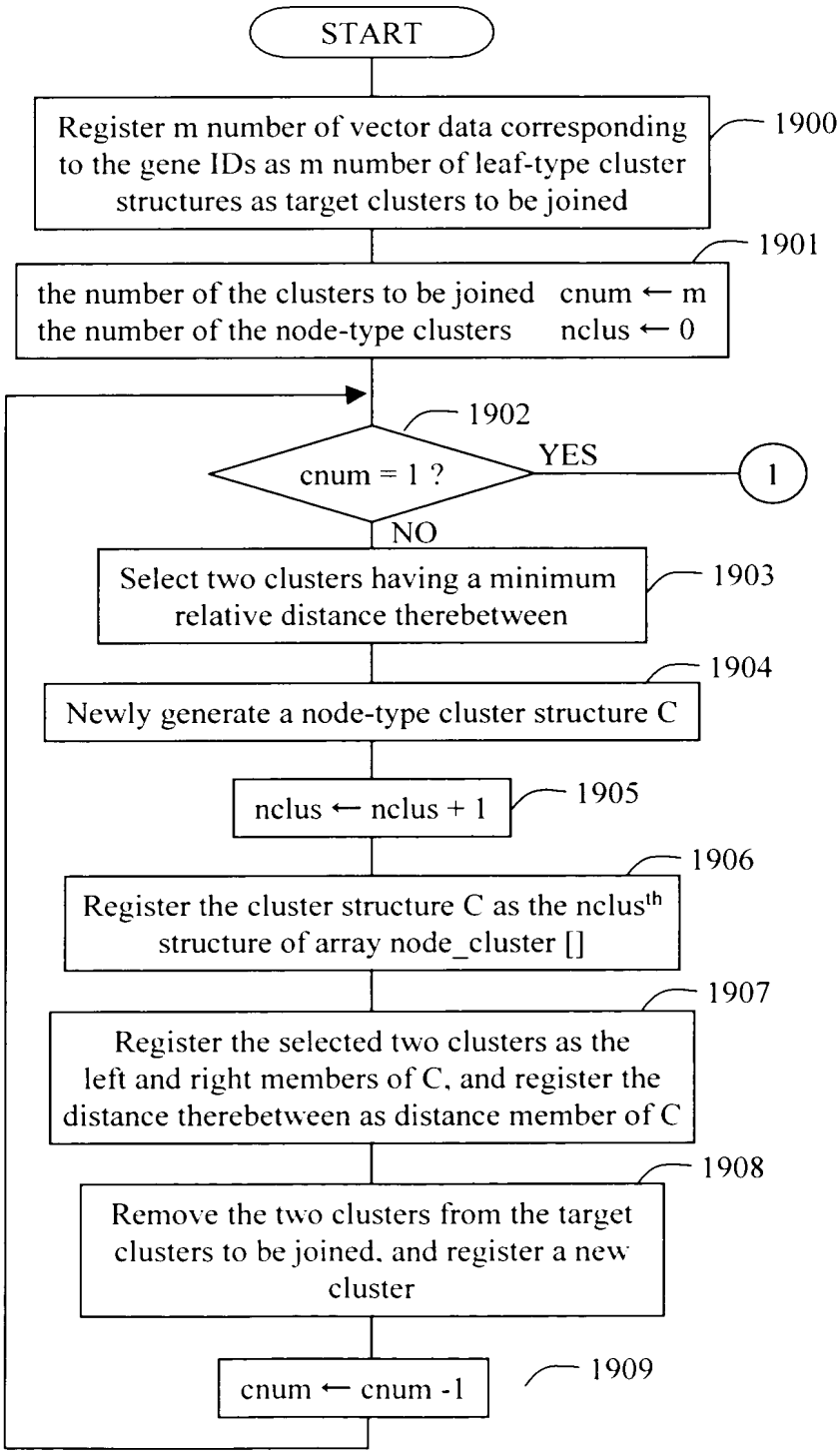

FIG.20

Detailed flowchart of clustering analysis (2: Setting cluster levels)

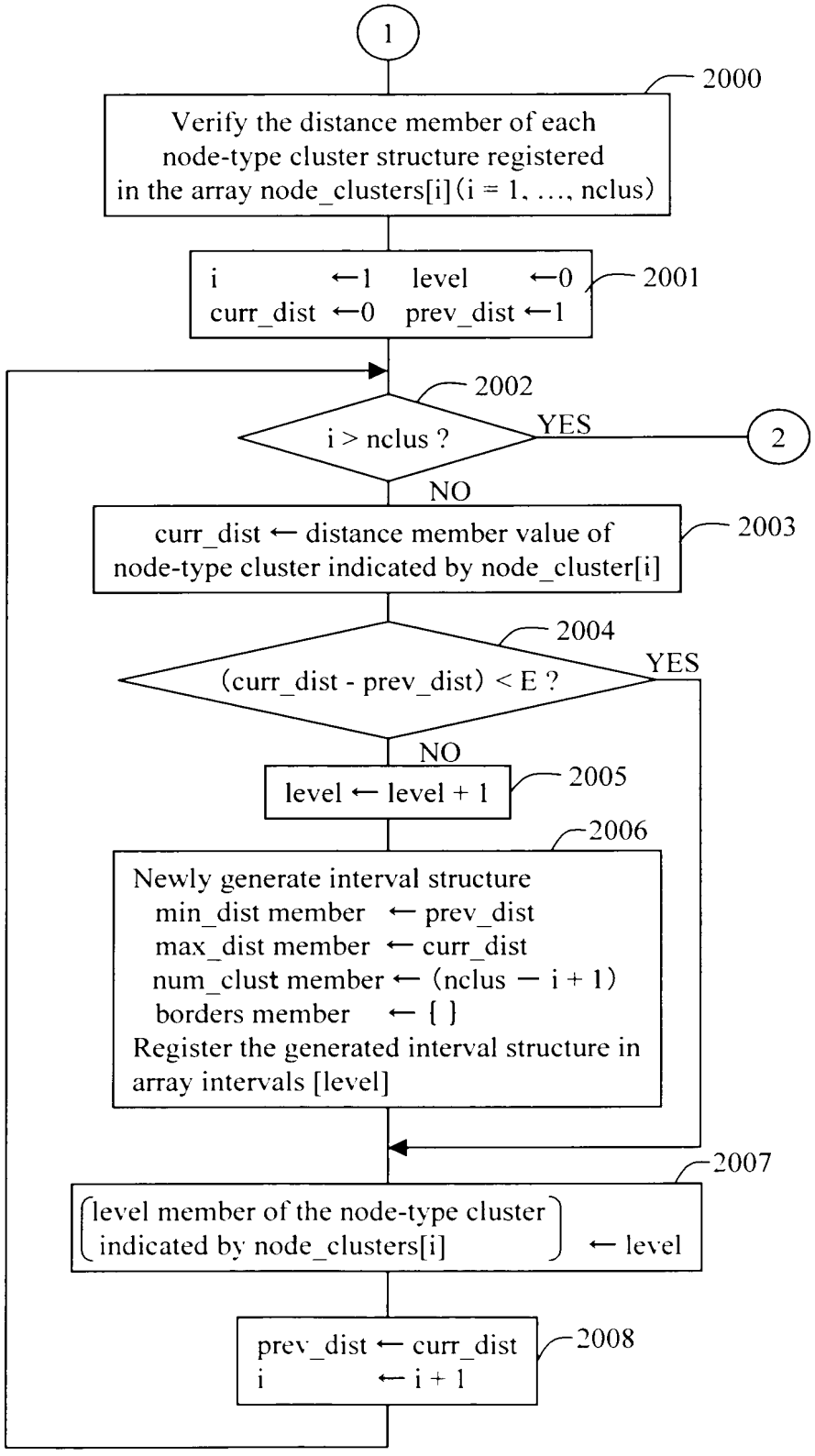

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FIG.21

Detailed flowchart of clustering analysis (3: Generating display data)

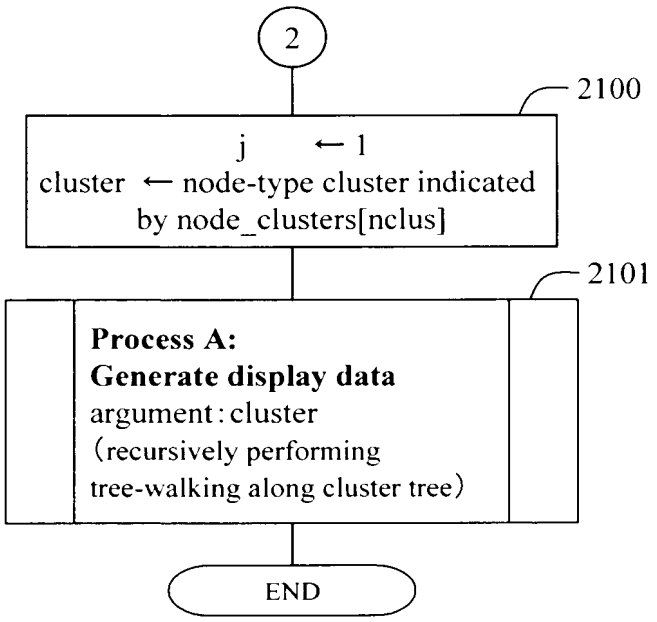

FIG.22

Flowchart of generating display data (Process A)

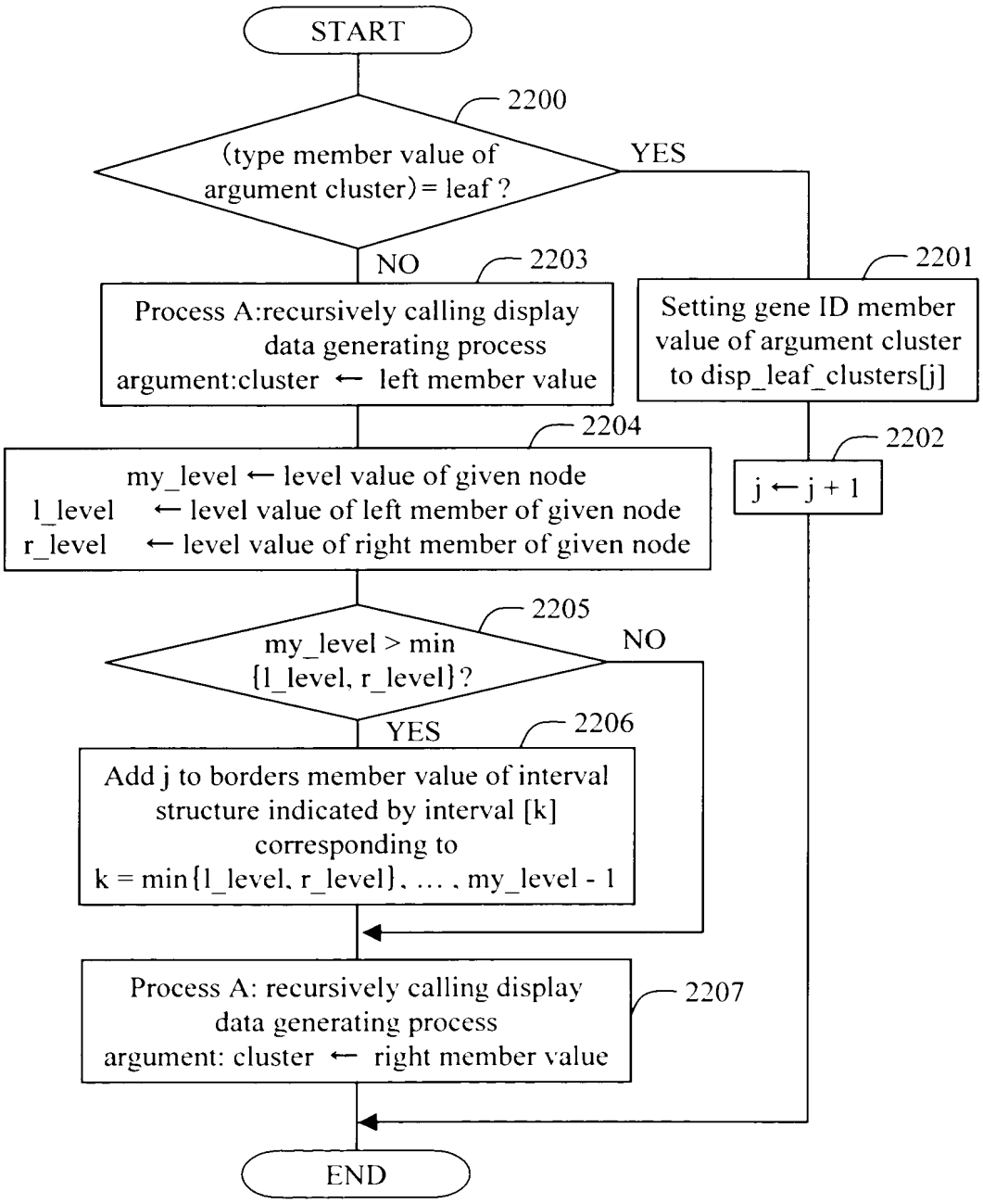

FIG.23

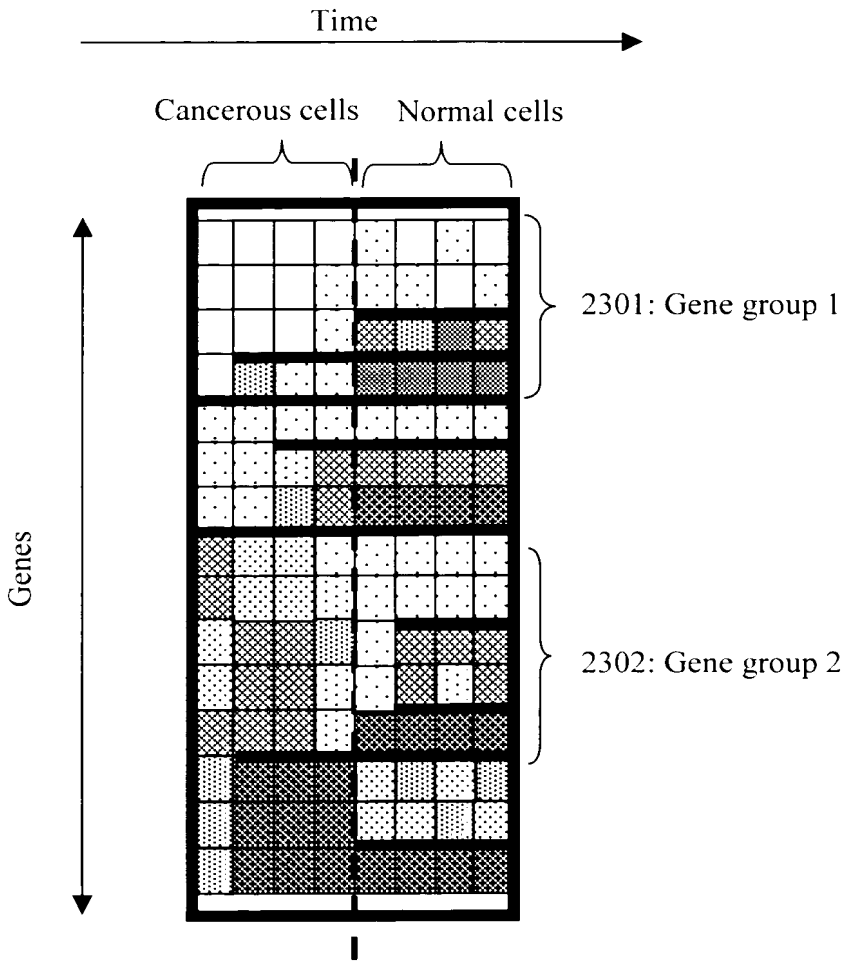
Time
Cancerous cells
Normal cells
Genes
2301: Gene group 1
2302: Gene group 2

FIG.24

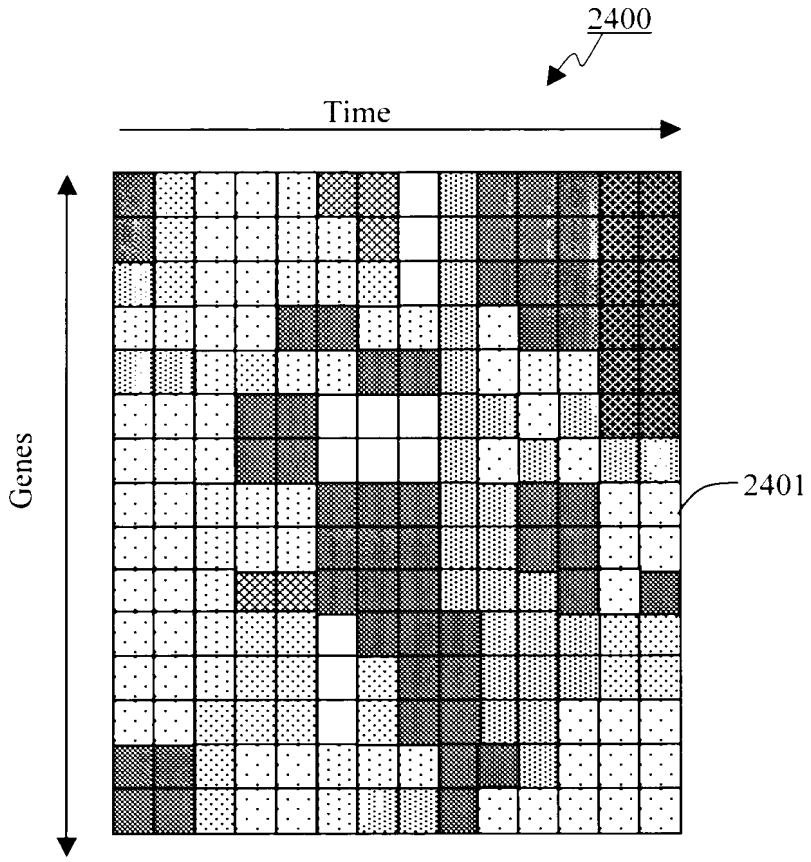

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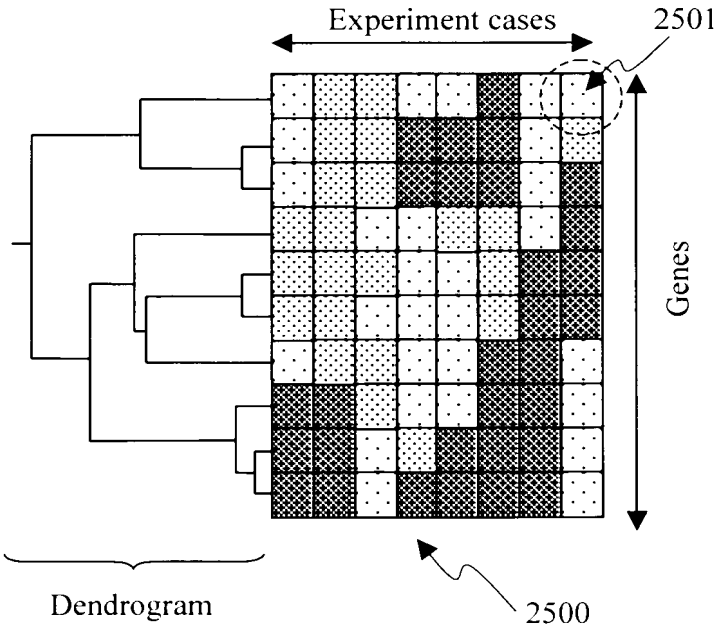
FIG.25

Exemplary display of standard clustering analysis



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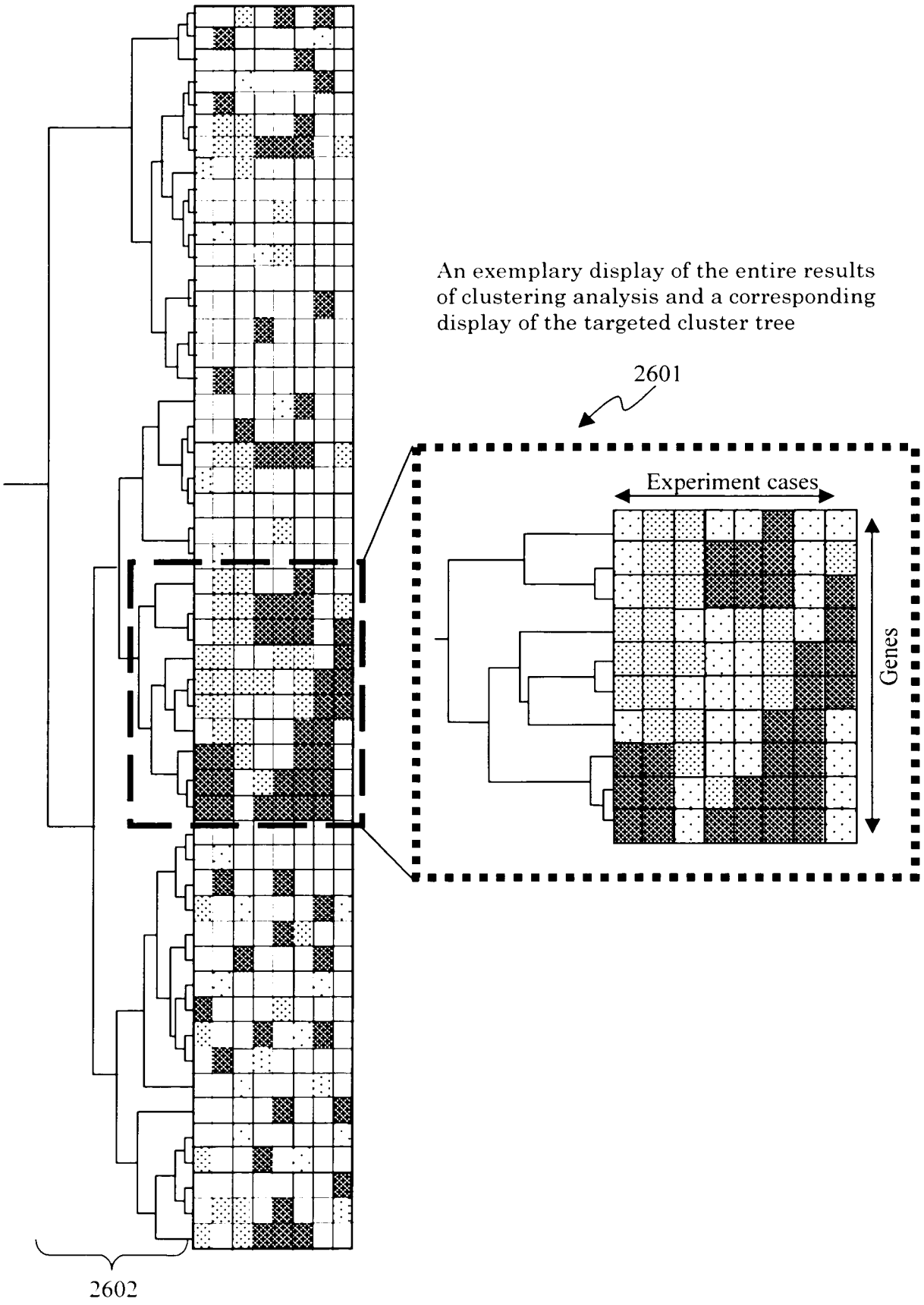
FIG.26